Chicago-Kent Law Review

Volume 78
Issue 1 *Symposium: Private Law, Punishment, and Disgorgement*

Article 15

April 2003

Federal Funding of Human Embryo Stem Cell Research: Advocating a Broader Approach

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FEDERAL FUNDING OF HUMAN EMBRYO STEM CELL RESEARCH: ADVOCATING A BROADER APPROACH

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INTRODUCTION

On August 9, 2001, in an historic evening television address to the nation, President George W. Bush announced a change in the long standing United States policy denying federal funding for human embryonic stem cell ("ES cell") research: federal funding would be made available for research on certain existing human ES cell lines.[1] In his address, President Bush told the American public that preliminary, privately-funded research has led many scientists to believe that further ES cell research "offers great promise that could help improve the lives of those who suffer from many terrible diseases—from juvenile diabetes to Alzheimer's, from Parkinson's to spinal cord injuries."[2] He also warned, however, that "[e]mbryonic stem cell research is at the leading edge of a series of moral hazards" and that "while we must devote enormous energy to conquering disease, it is equally important that we pay attention to the moral concerns raised by the new frontier of human embryo stem cell research. Even the most noble ends do not justify any means."[3]

These excerpts from President Bush's address frame the basic issues that must be faced when determining whether federal funds should be directed to human ES cell research. On one hand, ES cells have a seemingly enormous, though as of yet unproven, potential for use in developing medical treatments for some of mankind's most abhorred ailments. On the other hand, to create human ES cell lines, scientists must remove cells from a human embryo that is rendered

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1. President George W. Bush, *Remarks by the President on Stem Cell Research* (Aug. 9, 2001), *available at* http://www.whitehouse.gov/news/releases/2001/08/print/20010809-2.html.

2. *Id.*

3. *Id.*

nonviable by the process. This creates a prickly moral issue that raises concerns as to the correct characterization of an embryo and the overall value of human life, both for embryos and human beings afflicted with ailments that may prove susceptible to ES cell-derived treatments.

Federal funding is crucial to the success of human ES cell research. It serves both a pragmatic and symbolic function.[4] Pragmatically, it provides researchers with the necessary funding to continue and expand their work. Symbolically, it places a "stamp of approval" on the researchers' work and eases the transition of the technology into the mainstream. If human ES cell research is going to succeed in the United States, it needs federal funding.

This Note critiques President Bush's policy of federally funding ES cell research and concludes that too much of human ES cells' potential cannot be realized under the Bush plan. While the Bush plan is an improvement over a complete denial of federal funding for human ES cell research, its limiting of funding to research on a relatively small number of approved ES cell lines poses a significant obstacle to ES cell science. A more liberal plan of federal funding is needed, one that would fund not only research on existing stem cell lines, but also creation of and research on new ES cell lines.

A more liberal funding plan would give scientists the ability to transcend limitations that are inherent in existing stem cell lines, such as the lines' questionable viability[5] and unsuitability for use in developing transplantation products. It would also lead to a more diverse pool of ES cell lines that would allow researchers to work around existing intellectual property rights and to develop therapeutic products that could benefit the largest possible portion of the population. A more liberal funding plan would also benefit taxpayers because they would receive more effective and efficient research for their tax dollars.

Part I of this Note explains what an ES cell is, examines the potential uses of ES cells, and briefly outlines the ethical and moral issues surrounding ES cells. It also explores the importance of federal funding to ES cell research and outlines the Bush plan of federally funding human ES cell research as well as two alternative plans. Part II examines exactly how the Bush funding policy constrains ES cell

4. *See infra* Part I.D.

5. *See* Michael Lasalandra, *Government Scientists: 60 Stem Cell Lines Enough*, BOSTON HERALD, Aug. 11, 2001, at 8, *available at* 2001 WL 3808463.

science and medical research, focusing on four major concerns that illustrate the need for broader federal funding of human ES cell research. Finally, this Note concludes that a broader approach to federally funding human ES cell research is necessary if ES cell science is going to reach its full potential.

I. BACKGROUND

A. What Are Human Embryonic Stem Cells?[6]

Every living thing is made of cells.[7] The cell is one of the most fundamental units of life. Complex organisms such as humans are made up of millions of cells.[8] In these complex organisms, the cells are organized into tissues, the tissues are organized into organs, the organs are organized into organ systems, and the organ systems are organized into the organism.[9]

Over two hundred types of cells make up the human body.[10] These cells vary from blood cells to muscle cells to nerve cells.[11] But as different as these cells are, they all have the same ultimate origin: the totipotent[12] cells of the human embryo.[13] These totipotent cells have the ability to form any type of cell present in the human body. Additionally, each totipotent cell is capable of developing into a complete embryo.[14] In the course of normal embryological development, these totipotent cells give rise to genetically identical copies of themselves that, in turn, become the specialized cell types of the body

6. This Note can, of course, only skim the surface of the science behind ES cells. For a good review of the state of science of stem cell research, see DEP'T OF HEALTH AND HUMAN SERVS., STEM CELLS: SCIENTIFIC PROGRESS AND FUTURE RESEARCH DIRECTIONS (2001), *at* http://www.nih.gov/news/stemcell/fullrptstem.pdf.

7. ROBERT A. WALLACE, BIOLOGY 57 (7th ed. 1997).

8. The best current estimates are that the average human body is comprised of about 100 trillion cells. The Wellcome Trust, *A Genomics Primer*, http://www.wellcome.ac.uk/en/genome/thgpri.htm.

9. WALLACE, *supra* note 7, at 334–35.

10. BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL 36 (3d ed. 1994).

11. *See id.* at 36–37.

12. "Totipotent" is defined as "capable of developing into a complete embryo or organ[.]" WEBSTER'S NEW WORLD COLLEGE DICTIONARY 1512 (4th ed. 1999).

13. *See* ALBERTS, *supra* note 10, at 32 (stating that "[t]he cells of almost every multicellular organism are generated by repeated division from a single precursor cell.").

14. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at F-10.

by switching particular genes on or off.[15] The process by which cells go from stem cells to specialized cells is known as differentiation.[16]

ES cells are derived from these same totipotent cells of the early human embryo.[17] Up to the eight-cell stage of development, each cell of a mammalian embryo is totipotent.[18] The totipotent cells used to create ES cells are typically extracted from the inner cell mass of a day-five (postfertilization) human embryo known as a blastocyst, usually comprised of between two hundred and two hundred fifty cells.[19] This extraction process renders the embryo nonviable.

Rather than being totipotent, ES cells are pluripotent: they can give rise to differentiated cell types from the ectoderm, the endoderm, and the mesoderm, the three primary germ layers of the embryo.[20] During embryological development, the various cells of the human body arise from these three primary germ layers through further differentiation.[21] This means that an ES cell can differentiate into almost all of the cells of the body.[22] Human ES cells and human embryonic germ cells[23] ("EG cells") are the only known sources of pluripotent human stem cells,[24] leading many scientists to conclude that pluripotent ES cells offer greater promise than alternative stem

15. ALBERTS, *supra* note 10, at 34–35.

16. *Id.* at G-8 (defining differentiation as the "[p]rocess by which a cell undergoes a change to an overtly specialized cell type").

17. James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCI. 1145, 1145 (1998).

18. ALBERTS, *supra* note 10, at 1058.

19. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 13. These embryos can be fresh or frozen. *Id.* at C-1. Human embryos at the day-five blastocyst stage are also the embryos commonly used for implantation by in vitro fertilization ("IVF") clinics because this stage of development parallels the stage at which a human embryo would implant into the wall of the uterus in vivo. *Id.* at 13. This makes excess products of IVF an attractive source of embryos to be used in ES cell creation.

20. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 5.

21. WALLACE, *supra* note 7, at 311.

22. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 5.

23. Human EG cells are derived from the primordial germ cells of developing fetuses and embryos. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at ES-2. Other types of stem cells, such as adult stem cells or umbilical stem cells, are able to differentiate into some other types of cells, but are not pluripotent. *Id.* at ES-6. EG cells and ES cells are similar in many respects, but differ in their origins and growth characteristics. *Id.* at 14. EG cells are isolated from primordial germ cells extracted from the gonadal ridge (the precursor to the testes or ovaries) of a five- to ten-week fetus. *Id.* at ES-2. Also, EG cells have been maintained for only seventy to eighty population doublings in vitro, whereas ES cells have been maintained for several hundred population doublings. *Id.* at 14. In addition, EG cells show different differentiation characteristics than ES cells show. *Id.* at 14–15. Policies of federally funding human EG cell research is beyond the scope of this Note.

24. *Id.* at ES-1.

cell technologies such as adult stem cells or hematopoietic[25] stem cells.[26]

In addition to being pluripotent, ES cells are also capable of unlimited undifferentiated proliferation in vitro.[27] That is, ES cells, when cultured in the laboratory, will divide infinitely and will remain stem cells, as opposed to differentiating into specialized cell types. Human ES cells have been propagated in vitro for approximately two years and several hundred population doublings.[28] This characteristic makes it possible to use one ES cell to create an ES cell line. A cell line is an unlimited source of cells of a standardized, genetically homogenous type.[29] In other words, once you have one ES cell, you theoretically have an infinite supply of that ES cell that can be used for research, medical, or other purposes. These ES cell lines provide the human ES cells that researchers use for their work.

B. The Promise of Stem Cells

The intense interest in human ES cells comes from their potential medical uses. Because human ES cells are pluripotent, they can theoretically be manipulated into any human cell or even into any human tissue.[30] ES cells are viewed, therefore, as a potential source of replacement cells and tissues that could be used to repair damage caused by disease or injury.[31] For example, Israeli scientists recently announced that they had succeeded in transforming human ES cells into immature heart-tissue cells in their lab.[32] It has been estimated that three thousand Americans die every day from diseases that may

25. Some hematopoietic stem cells derive from umbilical cord blood and are sometimes referred to as umbilical stem cells. *See id.* at 46–47.

26. Stem cell technologies other than ES cells are beyond the scope of this Note. However, most researchers are keen to see both embryonic and adult stem cells pursued. As Art Caplan, a bioethicist at the University of Pennsylvania in Philadelphia, points out, placing bets on embryonic over adult stem cells, or vice versa, is like standing in the 18th century and trying to predict the future of aviation from watching a balloon and a kite. It is far too early in stem-cell technology to say which approach will ultimately fly. *Masters of Disguise*, THE ECONOMIST, Mar. 16, 2002, at 80–81, *available at* 2002 WL 7245517.

27. Thomson, *supra* note 17, at 1145.

28. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 14. Other types of stem cells, such as adult stem cells or umbilical stem cells, are able to differentiate into some other types of cells, i.e., they are multipotent, but are not pluripotent. *Id.* at ES-6.

29. ALBERTS, *supra* note 10, at 892–93.

30. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at ES-1.

31. *Id.*

32. Bill Hoffmann, *Doctors Turn Stem Cells to Heart Tissue*, N.Y. POST, Aug. 2, 2001, at 19.

be treatable in the future with therapies derived from ES cell research.[33]

There are also potential medical uses of human ES cells that do not involve transplantation. For example, human ES cells have been proposed as a way to study early events of human development.[34] Another proposed use of human ES cells is to test candidate therapeutic drugs and screen toxins.[35] Human ES cells also have potential use in developing new methods for genetic engineering.[36] Perhaps the medical potential of ES cells was best summed up when former NIH director Harold Varmus, testifying on stem cell technology before Congress, stated: "There is almost no realm of medicine that might not be touched by this innovation."[37]

C. *The Catch: Ethical and Moral Issues Regarding Human ES Cells*

Along with the incredible medical potential of human ES cells, however, comes a catch: serious ethical and moral concerns over human ES cells that arise from ES cells' origins. Current techniques for deriving human ES cells require extraction of cells from a human embryo, which leaves the embryo nonviable.[38] This fact has lead to widespread and outspoken opposition to research using human ES cells from, among others, prolife groups and the Catholic Church.[39] Their argument against ES cell research is analogous to their argument against abortion: life begins at conception, so the destruction of an embryo in the process of creating human ES cells is equivalent to killing any other human being.[40]

Opposite these ES cell opponents, the chief proponents of ES cell research[41] have been patients' groups representing individuals inflicted with the maladies for which ES cell technology seems to hold the most promise. The most notable ES cell proponents are Nancy

33. Robert P. Lanza et al., *The Ethical Reasons for Stem Cell Research*, 292 SCI. 1299 (2001).

34. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 17.

35. *Id.* at 17–18.

36. *Id.* at 18.

37. Anne McLaren, *Stem Cells: Golden Opportunities with Ethical Baggage*, 288 SCI. 1778 (2000).

38. *See, e.g.*, Thomson, *supra* note 17, at 1145 (1998).

39. *See* Alexander Morgan Capron, *Stem Cells: Ethics, Law and Politics*, 20 BIOTECHNOLOGY L. REP. 678, 687 (2001); Gretchen Vogel, *Bush Squeezes Between the Lines on Stem Cells*, 293 SCI. 1242 (2001).

40. Capron, *supra* note 39, at 687.

41. This ignores, of course, the scientific community with its vested interest.

Reagan[42], lobbying on behalf of Alzheimer's disease patients such as President Ronald Reagan; Christopher Reeve[43], lobbying on behalf of victims of spinal cord injuries; Mary Tyler Moore[44], lobbying on behalf of diabetes patients; and Michael J. Fox[45], lobbying on behalf of Parkinson's disease patients.[46]

These groups' argument for human ES cell research is as follows: the sacrifice of an unwanted human embryo is justifiable if done for the benefit of those human beings suffering from maladies treatable by ES cell-derived techniques.[47] This argument is echoed by some legislators who insist that supporting the destruction of human embryos for the purpose of developing lifesaving medical treatments is, in effect, a "prolife" position.[48]

Opponents of ES cell research counter with the fact that ES cells' medical promise is currently unproven.[49] This argument leaves ES cell researchers in a catch-22: researchers cannot get funding because ES cells' medical promise is unproven, and researchers cannot prove ES cells' promise because they cannot get funding. This catch-22 is unacceptable for something that has as much theoretical medical promise as ES cells.

Another point that proponents of ES cell research emphasize is that the embryos used to create ES cell lines are typically surplus embryos that were created by in vitro fertilization for reproductive purposes and are no longer needed.[50] Because these embryos, if not implanted, will simply be destroyed,[51] many question the harm in

42. Capron, *supra* note 39, at 681.

43. *Stars Lobby for Stem Cell*, CINCINNATI POST, Aug. 10, 2001, at A14, *available at* 2001 WL 24527290.

44. *Id.*

45. *Id.*

46. Support from luminaries such as these have turned stem cell research into "Hollywood's latest social cause." *Id.*

47. *See* Richard O. Hynes, *Prepared Testimony of Richard O. Hynes, Ph.D., President of the American Society for Cell Biology Before the Senate Appropriations Committee Labor, Health & Human Services Subcommittee Research*, Federal News Service, Sept. 14, 2000, *available at* 2000 WL 23832686.

48. Capron, *supra* note 39, at 681. Professor Capron also notes that this argument seems to resonate with much of the public.

49. *See* Brad Evenson, *Research Miracles Just Hype for Now*, NAT'L POST, Aug. 10, 2001, at A13, *available at* 2001 WL 25980519 ("The hope that stem cells could one day cure disease is so speculative that private companies have deemed it too risky [for investment].").

50. Hynes, *supra* note 47.

51. Each year thousands of embryos are destroyed at their progenitors' requests. Lanza, *supra* note 33, at 1299.

using them to benefit others.[52] The recent advent of embryo adoptions, however, has removed some of the poignancy from this point. Groups, such as Nightlight Children Adoptions' Snowflake program in Fullerton, California, are springing up that link infertile couples to couples that have excess embryos from IVF treatments.[53] The excess embryos are implanted in the donee mother and, in successful cases, the result is pregnancy and a child. While the number of excess embryos is currently far greater than the demand for embryo adoptions, some have predicted that the current ES cell controversy will lead to a bridging of that gap.[54]

President Bush summarized the ethical and moral concerns surrounding ES cell research well when he broke them down into two questions: "First, are these frozen human embryos human life, and therefore, something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they be used . . . for research that has the potential to save and improve other lives?"[55]

D. The Importance of Federal Funding to Human ES Cell Research

There are currently no limits on private funding of human ES cell research. Scientists working with private funding are free to conduct whatever research they want on whatever ES cell lines they want.[56] So why is the question of federal funding for human ES cell research such a pressing concern? There are two answers to this question. Government funding is critical to ES cell research both pragmatically, because it provides necessary resources, and symbolically, because it places the significant weight of the government behind the research.[57] Federal funding of ES cell research also gives

52. *See, e.g.*, Hynes, *supra* note 47. This approach is complicated, however, by the issue of embryo adoptions, which is addressed *infra*. *See* Jennifer Bayot, *New Faces in Stem Cell Debate: Foes of Research Cite Embryonic Adoptions*, BOSTON GLOBE, July 18, 2001, at A1, *available at* 2001 WL 3942817.

53. Bayot, *supra* note 52, at A1.

54. *Id.*

55. President George W. Bush, *supra* note 1.

56. *See* Vogel, *supra* note 39. A few states do have laws that act as barriers to stem cell research, but these are largely inconsequential.

57. *See* ANDREA L. BONNICKSEN, IN VITRO FERTILIZATION: BUILDING POLICY FROM LABORATORIES TO LEGISLATURES 100 (1989) ("Affirmative policy eases techniques symbolically, by placing the weight of the government behind them, or pragmatically, by allocating resources for their use.").

the government more control over the ES cell researchers and the direction of ES cell research.[58]

Pragmatically, federal funding is perceived as crucial to almost all basic research. In fact, federal funding accounts for about 85 percent of sponsored research expenditures in the United States.[59] ES cell research is currently being stifled by a lack of funding.[60] Although private funding for human ES cell research should be increasingly forthcoming as ES cell science comes closer to reaching its potential, at this early stage of ES cell research, federal funding is imperative for significant progress.[61]

Symbolically, federal funding seems to reflect some sort of government, and therefore public, stamp of approval on funded research.[62] By providing federal funding for human ES cell research, the government confers legitimacy on ES cell science and eases its transition into the mainstream.[63]

The government also increases its control over ES cell science when it provides federal funding.[64] ES cell research grant proposals seeking federal funds must face a government review panel which functions as an independent review by specialized experts; an ES cell researcher using only private funds, however, needs only satisfy a review by an in-house review board whose review is often cursory.[65] This gives the government the opportunity to make sure that only efficient and effective research is being conducted. If the reviews are properly conducted, taxpayers benefit by getting more research bang

58. *See id.* at 107.

59. ASS'N OF UNIV. TECH. MANAGERS, AUTM LICENSING SURVEY: FY 1999, SURVEY SUMMARY 1 (2000), *at* http://www.autm.net/surveys/99/survey99A.pdf.

60. *See* Evenson, *supra* note 49.

61. *But see* Capron, *supra* note 39, at 697.

> Jim Clark, founder of several Silicon Valley companies, has decided to withhold $60 million of the $150 million he had pledged to Stanford University for a center for biomedical engineering and science because he has concluded that the politicization of stem cell research in the United States means that the "new future for medicine and biology and for resulting entrepreneurship" that he had intended to stimulate at Stanford will instead occur abroad, especially in the U.K.

Id. For a parallel problem, see the discussion of the flight of scientists in Part II.B.

62. *See* BONNICKSEN, *supra* note 57, at 100–16. Professor Bonnicksen addresses federal funding and legislation of IVF in its early days. The position of IVF at that stage is analogous to the position that ES cell science is in right now.

63. *Id.* at 101.

64. "[F]ederal funding [is] a double-edged sword for the researcher. It brings in dollars to support research but also opens the project to regulation and control." *Id.* at 107.

65. *Id.*

for their tax buck, and ES cell science benefits by being steered towards the most effective and efficient avenues.

Federal funding is crucial to ES cell science's success. It provides necessary pragmatic and symbolic support for the research and subjects ES cell science to a degree of government control, which, if properly exercised, will benefit ES cell science.

E. The Bush Plan to Federally Fund Human ES Cell Research and Alternative Plans

President Bush's plan, currently followed by the NIH in distributing research dollars, allows federal funding of research on human ES cell lines that existed prior to his August 9, 2001 announcement, but withholds federal funding from research on any human ES cell lines derived after this date.[66] To be eligible for federal funding, the human ES cell lines must also have been derived from embryos that were created for fertility treatments but are no longer needed, and the embryos must have come from couples that gave their informed consent free of any financial inducements.[67] The NIH initially released a list of sixty-four human ES cell lines ("approved ES cell lines") that meet these criteria.[68] The number of approved ES cell lines has, however, subsequently increased to seventy-eight and may be subject to even further upward revision.[69] Research on any other human ES cell lines is not eligible for federal funding under Bush's plan.

President Bush's plan marks a departure from long standing United States policy that acted as a de facto ban on federal funding of human ES cell research.[70] ES cell research opponents would like to

66. Vogel, *supra* note 39, at 1242.

67. *Id.* at 1243.

68. NATIONAL INSTITUTES OF HEALTH (NIH), UPDATE ON EXISTING HUMAN EMBRYONIC STEM CELLS (Aug. 27, 2001), *at* http://www.nih.gov/news/stemcell/082701list.htm.

69. NIH Human Embryonic Stem Cell Registry, http://escr.nih.gov.

70. In 1993, shortly after entering office, President Clinton ordered the repeal of a moratorium, issued during the presidency of George H. W. Bush, on federal funding of certain fetal tissue research. Federal Funding of Fetal Tissue Transplantation Research, 58 Fed. Reg. 7457 (Jan. 22, 1993). Congress added legislative force to the repeal of the moratorium with the passage of the NIH Revitalization Act of 1993, which also created statutory guidelines governing fetal tissue transplantation. Pub. L. No. 103–43, Title I(A), 107 Stat. 122, 126–33 (codified at 42 U.S.C. §§ 289g, 289g-1, 289g-2). While up until this point federal funding for human ES cell research would have been relatively uninhibited, Congress followed the NIH Revitalization Act of 1993 with the 1996 enactment of the "Dickey Amendment," a rider to an appropriations bill, that unambiguously prohibited research resulting in the destruction of embryos. The Balanced Budget Downpayment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26

see a reversion to this state once again. At least one congressman, Representative Ron Lewis (R-KY), has indicated that he might introduce a bill that would unambiguously ban federal funding of human ES cell research.[71] It seems unlikely that any such bill would ever become law, however, because it appears that a sizable majority of Congress supports at least some federal funding for human ES cell research.[72]

This Note advocates enacting a plan for federally funding human ES cell research that is broader than the Bush plan. What is particularly needed is funding of research on stem cell lines created after the cutoff date set by the Bush plan. One bill that set forth such a plan was the New Century Health Advantage Act.[73] This bill would have removed all statutory limitations on federal funding of human ES cell research.[74] Although this bill is now moot due to the expiration of the legislation it sought to repeal (the Dickey Amendment[75]), it is a useful example because of the very broad funding approach that it proposes.

II. THE SHORTCOMINGS OF THE BUSH PLAN

The Bush plan will allow researchers to conduct much of the basic ES cell research that is needed, but it will not allow the researchers to reach their end goal, revolutionary medical applications of this technology. While there is something to be said for President Bush's

(1996). The Dickey Amendment has been reenacted annually. *See* Consolidated Appropriations—FY 2001, Pub. L. No. 106-554, §510, 114 Stat. 2763 (2000). It should be noted that President Clinton, later in the second term of his presidency, supported a Department of Health and Human Services ("HHS") interpretation of the Dickey Amendment that would have allowed funding for research on human ES cells as long as the ES cells were obtained from private sources; however, this approach to federally funding human ES cell research was never utilized. *See* Jason H. Casell, Note, *Lengthening the Stem: Allowing Federally Funded Researchers to Derive Human Pluripotent Stem Cells from Embryos*, 34 U. MICH. J.L. REFORM 547, 566–67 (2001); Judy Holland, *Scientists Fear Loss of Stem Cell Funds*, MILWAUKEE J. SENTINEL, Jan. 15, 2001, at A1, *available at* 2001 WL 9333428. Therefore, the practical effect on federal funding of human ES cell research was an absolute ban. For an overview of federal funding of fetal research in the pre-Clinton years, see Capron, *supra* note 39, at 682–83.

71. Sheryl Henderson Blunt, *Embryos Split Prolifers*, CHRISTIANITY TODAY, Sept. 3, 2001, *available at* 2001 WL 10317801.

72. *See, e.g.*, *id.*; *see also* Lee Davidson, *Bennet Supports Stem-Cell Research*, DESERT NEWS, July 21, 2001, at A1, *available at* 2001 WL 24492908.

73. H.R. 2838, 107th Cong. (2001). The Stem Cell Research Act of 2001, currently in both the House of Representatives and the Senate, advocates a similar position but sets some restrictions upon embryos that can be used and prohibits funding of research resulting in human cloning or the creation of human embryos. H.R. 2059, 107th Cong. (2001); S. 723, 107th Cong. (2001).

74. H.R. 2838, 107th Cong. (2001).

75. See *supra* note 70.

political "splitting the baby,"[76] his plan is not an acceptable long-term solution. This Section sets forth four specific shortcomings of the Bush plan, and shows how a broader plan of funding would remedy these shortcomings.

A. Property Rights

One shortcoming of the Bush plan is that by limiting research funding to seventy-eight existing human ES cell lines,[77] it artificially constrains the market for these cell lines, and, consequently, inflates the value of property rights in these cell lines. This is due simply to the law of supply and demand.[78] A broader plan of federal funding, one that allows funding for later derived ES cell lines as well, would broaden the pool of ES cell lines available to researchers and, therefore, would decrease the value of property rights in ES cells.

1. The Obstacles that Property Rights Create

The problems that property rights in the approved ES cell lines will create for researchers are already becoming clear. Officials from BresaGen, an Australia-based biotechnology company that has four human ES cell lines that qualify for federal funding under President Bush's plan, recently announced that they will make BresaGen's ES cell lines available to academic researchers at no charge.[79] These ES cell lines, however, will be far from free. Allan Robbins, BresaGen's senior vice president and chief scientific officer, has explained that the ES cell lines will be made available to the researchers for "no upfront payment in exchange for some first right of refusal for any intellectual property that researchers invent."[80] Similarly, the Wisconsin Alumni Research Foundation ("WARF"), a company formed to patent research discoveries at the University of Wisconsin, Madison, has agreed to make its ES cell lines available to NIH researchers and researchers at nonprofit institutions that receive NIH grants for a

76. *See, e.g.*, Vogel, *supra* note 39.

77. These seventy-eight lines are owned by just fourteen organizations. Göteborg University in Sweden holds the largest number of approved lines with nineteen. NIH Human Embryonic Stem Cell Registry, http://escr.nih.gov.

78. *See* RICHARD A. POSNER, ECONOMIC ANALYSIS OF LAW 9 (3d ed. 1986).

79. Tim Friend, *Free Stem-Cell Lines Will Be Offered to Researchers*, USA TODAY, August 22, 2001, at D10.

80. *Id.*

nominal fee to cover handling and distribution expenses. However, WARF will retain all commercial rights to the materials.[81]

The most valuable property rights that the fourteen owners of approved ES cell lines have are the intellectual property rights in the cell lines. It is these intellectual property rights that will most hinder ES cell science.

Illustrative of the problems caused by intellectual property rights in the approved human ES cell lines is a patent owned by WARF, U.S. Patent No. 6,200,806 ("'806 patent").[82] The inventor of WARF's '806 patent is Dr. James A. Thomson, a University of Wisconsin researcher who was the first individual to isolate human ES cells.[83] WARF's '806 patent claims human ES cells with various enumerated characteristics, two methods for isolating human ES cells, and a cell line developed using one of the claimed methods.[84] WARF clearly has full property rights, both personal and intellectual, in five human ES cell lines that it developed that meet requirements for federal funding under President Bush's plan. Based upon the eleven claims of the '806 patent, however, WARF is claiming intellectual property rights in every human ES cell line that qualifies for federal funding under President Bush's plan.[85] And there may well be merit to that claim.[86]

WARF's broad claims of intellectual property rights in the human ES cell lines has led would-be major players in ES cell science to scramble to negotiate with WARF. WiCell Research Institute, Inc., a company formed by WARF to handle its ES cell lines, and the Public Health Service ("PHS") of the United States Department of Health and Human Services recently signed a Memorandum of Understanding ("MOU") for research use of WiCell's (WARF's) existing patent rights and five human ES cell lines that are eligible for federal research funding under President Bush's plan.[87]

81. News Release, National Institutes of Health, National Institutes of Health and WiCell Research Institute, Inc., Sign Stem Cell Agreement (Sept. 5, 2001), *at* http://www.nih.gov/news/pr/sep2001/od-05.htm [hereinafter NIH].

82. (issued Mar. 13, 2001); *see also* U.S. Patent No. 5,843,780 (issued Dec. 1, 1998).

83. *See* Thomson, *supra* note 17.

84. U.S. Patent No. 6,200,806 (issued Mar. 13, 2001); *see also* U.S. Patent No. 5,843,780 (issued Dec. 1, 1998).

85. *See* Friend, *supra* note 79.

86. *See* Michael D. Lemonick, *Keeper of the Stem Cells: Now That There's Federal Money for Research, Can Patent Holders Meet Demand for the Precious Lines?*, TIME, Aug. 27, 2001, at 57.

87. NIH, *supra* note 81. A copy of the Memorandum of Understanding is available online at http://www.nih.gov/news/stemcell/WicellMOU.pdf.

The MOU has two parts, one dealing with use of WARF's patent rights, and one dealing with use of WARF's approved ES cell lines. The first part of the MOU provides that WiCell allow PHS to use its patent rights in research involving WARF's approved ES cell lines and third-party-approved cell lines[88] and grants third parties supplying approved ES cell lines to PHS researchers "a limited, revocable, non-commercial, research license" to WARF's patent rights.[89] The first part of the MOU also gives WiCell reach through intellectual property rights in any commercial products that stem from PHS's research.[90]

The second part of the MOU allows PHS researchers to use WARF's five approved ES cell lines subject to the following conditions: ownership of the ES cell lines shall remain with WiCell;[91] the ES cell lines are not to be used for diagnostic or therapeutic purposes;[92] the ES cell lines must be used in compliance with applicable statutes, regulations, and guidelines;[93] and the ES cell lines are only to be used for teaching or noncommercial research purposes.[94] The second part of the MOU also grants WiCell reach through intellectual property rights to commercial products that are created with their approved ES cell lines.[95] WARF will extend the same terms from the

88. Memorandum of Understanding Between WiCell Research Institute, Inc. and Public Health Service, U.S. Department of Health and Human Services § 1(a-b) (Sept. 5, 2001), *available at* http://www.nih.gov/news/stemcell/WicellMOU.pdf.

89. The license only applies when the third-party-approved lines are used for teaching or noncommercial research purposes. Commercial use of third party lines requires a separate licensing agreement with WiCell or WARF. *Id.* at § 1(c).

90. Section 1(d) of the MOU provides:

> The Parties recognize that Wisconsin Patent Rights may be used in PHS research to make patentable discoveries ("PHS Patent Rights"), which themselves may eventually be the basis of commercial products that benefit public health. Any grant of Wisconsin Patent Rights that may be needed by a third party for commercialization of PHS Patent Rights shall be done by a separate written agreement with WiCell permitting such use of Wisconsin Patent Rights under terms not less favorable than other similar commercial licenses to the extent such rights are available.

Id. at § 1(d).

91. *Id.* at § 2(a).

92. *Id.* at § 2(b).

93. *Id.* at § 2(c).

94. Commercial use of the ES cell lines requires a separate agreement with WiCell. *Id.* at § 2(d).

95. Section 2(h) of the MOU provides:

> The Parties recognize that Wisconsin Materials may be used in the PHS research program to make discoveries of different materials ("PHS Materials") which themselves may eventually be the basis of commercial products that benefit public health. Any grant of rights to Wisconsin Materials or Wisconsin Patent Rights that may be needed by a third party for commercialization of PHS Materials shall be done by a separate written agreement with WiCell permitting such use of Wisconsin Materials or Wiscon-

MOU, which governs only technology transfer to PHS (NIH) researchers, to researchers at nonprofit institutions that receive grants from NIH, provided those researchers enter a separate written agreement with WiCell.[96]

WARF's '806 patent potentially makes it the gatekeeper through which all use of ES cells approved for federal research funding under President Bush's plan must pass.[97] And this gatekeeper is not a disinterested party; WARF's five approved human ES cell lines are direct competitors of the other approved lines. WARF has said that it intends to make all ES cell lines covered by its '806 patent widely available to publicly funded researchers, but this gatekeeper role seems like a dangerous amount of power to be held by a single entity with a financial interest in five of the approved lines.[98]

When ES cell science reaches the point where commercial medical products are ready to be developed and made publicly available, intellectual property rights will pose a formidable obstacle, spawning litigation that could delay medical applications of ES cell science. Illustrative of this is a suit recently filed in the United States District Court for the Western District of Wisconsin by WARF against Geron, a Menlo Park, California, biotechnology company that was WARF's partner in the research that led to the '806 patent.[99] In this suit, WARF and Geron are wrestling for control over commercial rights to develop products from cell types that can be made from human ES cells.[100] Geron holds exclusive commercial rights to WARF's patent rights and approved ES cell lines to develop products from six cell types, including nerves, liver, and heart muscle.[101] Geron also has an option to add exclusive commercial rights to twelve more cell types that it wishes to exercise.[102] WARF has sued Geron to block Geron's exercise of that option.[103] Every cell type to which Geron holds an exclusive commercial right is, of course, a type that

sin Patent Rights under terms not less favorable than other similar commercial licenses to the extent such rights are available.

Id. at § 2(h).

96. *Id.* at § 4; NIH, *supra* note 81.

97. *See* Lemonick, *supra* note 86.

98. *See id.*; Friend, *supra* note 79.

99. Antonio Regalado & David P. Hamilton, *Geron is Sued over Control of Stem Cells*, WALL ST. J., Aug. 14, 2001, at A3.

100. *Id.*

101. *Id.*

102. *Id.*

103. *Id.*

WARF is not free to commercially license to other entities. This is very high stakes litigation. Somewhere down the road, the scope of WARF's '806 patent will probably also need to be litigated. All of this litigation slows down ES cell research and wastes resources that could be devoted to furthering that research.

2. Methods of Avoiding the Obstacles Created by Property Rights

Companies have begun developing ways to work around WARF's '806 patent. For example, BresaGen has reported that it has applied for a patent on a new method of isolating ES cells that would not infringe WARF's '806 patent.[104] BresaGen has not yet used the method to isolate human ES cells, but it hopes to do so soon.[105] But, of course, human ES cell lines developed with these new techniques will not be eligible for federal research funding under President Bush's plan.

This is a major reason why the government policy of funding ES cell research needs to be broadened. A broader funding approach would give government-funded researchers the flexibility to work around existing property rights in human ES cell lines. Researchers would be free to develop new methods of deriving ES cell lines that would allow them to circumvent existing intellectual property rights. This would result in cheaper research and, eventually, less expensive medical applications. It would also eliminate the possibility that a single patent holder could hold up all government-funded ES cell research.

B. Flight of Scientists

Another consequence of the funding limitations imposed by the Bush plan for human ES cell research funding is the effect that it has on where scientists choose to live and work. Simply put, scientists will choose to locate themselves in places that are conducive to their work. Obviously, the availability of government research funding is a factor in determining a location's conduciveness. There are also other less obvious burdens that accompany the denial of federal research funding for human ES cell research. For instance, the NIH is very careful to make sure that there is no intermingling between federally funded research and ES cell research that is barred from

104. Friend, *supra* note 79.
105. *Id.*

federal funding.[106] This has forced many scientists to segregate their human ES cell work completely from their other work, often being forced to move it off campus, even in cases where the scientist offers to reimburse the NIH for any overhead costs human ES cell projects share with other work.[107]

Due to frustration from restrictive funding of ES cell research, Roger Pedersen, formerly of the University of California, San Francisco, announced in July 2001 that he was leaving the United States and emigrating to Great Britain where he felt he would enjoy "the possibility of carrying out [his] research with human embryonic stem cells with public support."[108] Dr. Pedersen made his announcement on the heels of President Bush's announcement of his new human ES cell research funding policy and Great Britain's Medical Research Council's announcement that it would create a stem cell bank that uses spare embryos donated by thousands of couples undergoing IVF treatment.[109] In an article explaining his emigration, Dr. Pedersen wrote that the Bush plan for federal funding only on existing human ES cell lines "confer[s] an advantage on countries such as Britain and Canada, where there is government support for a wider range of stem cell research activities."[110] Dr. Pedersen also warned: "The potential benefits of stem cell research promise to transform healthcare and stimulate economic growth. But they will accrue to countries where the policies and funding encourage, rather than hobble, the stem cell enterprise."[111]

Indications are that Dr. Pedersen's departure may be the first drop in a flood should the United States federal ES cell research funding policy remain unchanged.[112] It already appears that the

106. Aaron Zitner, *Uncertainty Is Thwarting Stem Cell Researchers Policy: A Top Scientist is Leaving for Britain, as Human Embryo Cell Funding in U.S. Remains Unsolved*, L.A. TIMES, July 16, 2001, at A1.

107. *Id.*

108. *Id.*

109. David Firn, *Professor Warns US Will Miss Out over Stem Cells*, FIN. TIMES, Aug. 15, 2001, at 1, *available at* 2001 WL 25577487.

110. Roger Pedersen, *A Better Culture for Stem Cell Research*, FIN. TIMES, Aug. 15, 2001, at 15.

111. *Id.*

112. *See* Anthony Shadid, *Stem Cell Researchers Mull Move Overseas*, BOSTON GLOBE, August 9, 2001, at A1. Similarly, the United States may see an emigration of private research funds.

> Jim Clark, founder of several Silicon Valley companies, has decided to withhold $60 million of the $150 million he had pledged to Stanford University for a center for biomedical engineering and science because he has concluded that the politicization of stem cell research in the United States means that the "new future for medicine and

United States may not be at the front of ES cell science: only twenty-seven of the seventy-eight cell lines approved for funding under the Bush plan belong to organizations in the United States.[113] ES cell science in the United States will suffer further losses if federal funding of human ES cell research is not broadened.

C. *Limited Diversity of ES Cell Lines as an Obstacle to Developing Transplantation Products*

Another shortcoming of the Bush plan is that by only allowing funding of research on seventy-eight existing human ES cell lines, it places obvious constraints on the diversity of the cell lines. Diversity of human ES cell lines figures to be particularly valuable to the development of transplantable products from the ES cell lines, a major end goal of ES cell science.[114]

As with any transplantation technology, a major concern of using human ES cell-derived transplantation products is the potential for immune rejection.[115] Human cells express cell-surface proteins known as human-leukocyte-associated ("HLA") antigens.[116] The genes that code for these HLA antigens are highly polymorphic; that is, it is very rare for two individuals, save two identical twins, to have an identical set of HLA antigens.[117] The human immune system uses these HLA antigens to identify cells as either belonging to the body or as foreign.[118] Cells identified as foreign, the ones with HLA antigens different from those of the body's cells, are attacked by the immune system.[119] This immune response poses a serious obstacle to transplant procedures.[120] A key to success in creating transplantable products from human ES cell lines will be matching HLA antigens of the transplant recipient as closely as possible.[121] Success in matching

biology and for resulting entrepreneurship" that he had intended to stimulate at Stanford will instead occur abroad, especially in the U.K.

Capron, *supra* note 39, at 697

113. NIH Human Embryonic Stem Cell Registry, http://escr.nih.gov/.

114. *See* Ceci Connolly et al., *Viability of Stem Cell Plan Doubted*, WASH. POST, August 20, 2001, at A1.

115. DEP'T OF HEALTH AND HUMAN SVCS., *supra* note 6, at 17.

116. ALBERTS, *supra* note 10, at 1229–30.

117. *Id.* at 1230.

118. *See id.* at 1229–30.

119. *Id.* at 1230.

120. *Id.* at 1229–30

121. *See* Connolly et al., *supra* note 114. Another potential way around the problem of HLA antigens and rejection is the use of somatic cell nuclear transfer technology ("therapeutic

HLA antigens as closely as possible to transplant recipients will be directly proportional to the genetic diversity of available human ES cell lines.

Additionally, it appears that the vast majority of the seventy-eight human ES cell lines meeting President Bush's criteria for federal funding were derived from embryos from Caucasian couples, and a few were derived from embryos of Asian couples.[122] While the correlation between racial diversity and genetic diversity is debatable, this homogenous selection should at least raise some eyebrows.[123] Perhaps the most odious concern created by this lack of racial diversity is the possibility of the discriminatory availability of ES cell treatments. While current HHS Secretary Tommy Thompson has assured the public that the private sector will fill any voids in the current diversity of available ES cell lines, it seems unlikely that private companies would be clamoring to develop ES cell products tailored to minority populations because of a lack of financial incentives.[124]

In order to meet the major end goal of creating transplantation products using ES cell technology, ES cell scientists need as large a pool of ES cell lines as is possible. The Bush plan limits that pool to seventy-eight ES cell lines. A broader plan to federally fund human ES cell research, however, would significantly increase that pool, thereby increasing scientists' chance of meeting their end goals.

D. Xenotransplantation Concerns

Researchers face another substantial obstacle to meeting their end goal of developing transplantation products from ES cell technology: the Food and Drug Administration's ("FDA's") xenotransplantation guidelines. It appears that transplantation products derived from the seventy-eight Bush-approved ES cell lines would be barred from use in humans by these guidelines.[125] A broader plan of

cloning"). DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6. The very controversial topic of therapeutic cloning is beyond the scope of this Note.

122. Jon Entine & Sally Satel, *Inserting Race into the Stem Cell Debate*, WASH. POST, Sept. 9, 2001, at B1.

123. *See id.*

124. *Id.*; *see* Connolly et al., *supra* note 114.

125. *See* FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: SOURCE ANIMAL, PRODUCT, PRECLINICAL, AND CLINICAL ISSUES CONCERNING THE USE OF XENOTRANSPLANTATION PRODUCTS IN HUMANS 6 (2001), *available at* http://www.fda.gov/cber/gdlns/clinxeno0201.pdf; Justin Gillis & Ceci Connolly, *Stem Cell Research Faces FDA Hurdle*, WASH. POST, Aug. 24, 2001, at A1.

federally funding human ES cell research would allow researchers to develop transplantation products from new ES cell lines that would meet FDA xenotransplantation guidelines.

Xenotransplantation is defined by the FDA as "any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs."[126] Concerns over the possibility of the introduction and spread of infectious agents of animal origin into the human population have led to the FDA's creation of guidelines for the use of xenotransplantation products in humans.[127] These guidelines place very stringent limits on using any xenotransplantation products in humans. While these guidelines have been released in draft form only, the FDA is currently following them.[128]

It is believed that all existing human ES cell lines that meet President Bush's criteria for federal research funding are "xenotransplantation products" under FDA guidelines, and would therefore be subject to the guidelines' stringent restrictions.[129] This is because these ES cell lines were all grown using mouse feeder cells and bovine serum.[130] A technique for maintaining ES cell lines without using mouse feeder cells or bovine serum has recently been developed,[131] but any new ES cell lines developed and maintained with this technique would not be eligible for federal funding under President Bush's plan.

The magnitude of the obstacle that the FDA xenotransplantation guidelines place in front of human ES cell research funded under President Bush's plan is unclear. Harvard Medical School surgeon Hugh Auchincloss, Jr., chairman of an FDA committee that reviewed the xenotransplantation issue, has stated that the FDA xenotrans-

126. FOOD & DRUG ADMIN., *supra* note 125, at 6.

127. *Id.* at 2; *see* DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 95. An example of the introduction of an infectious agent of animal origin into the human population is the infamous bovine spongiform encephalopathy, better known as mad cow disease, and its human equivalent Creutzfeldt-Jakob disease. *Id.*

128. Gillis & Connolly, *supra* note 125.

129. *See id.*; *see also* FOOD & DRUG ADMIN., *supra* note 125, at 6.

130. DEP'T OF HEALTH AND HUMAN SERVS., *supra* note 6, at 95–96; Jill Carroll & Jim VandeHei, *Mouse Cells in Stem Lines May Limit Use*, WALL ST. J., Aug. 24, 2001, at A3.

131. *See* Chunhui Xu et al., *Feeder-Free Growth of Undifferentiated Human Embryonic Stem Cells*, 19 NATURE BIOTECHNOLOGY 971 (2001).

plantation policy is stringent but is not an absolute bar to research.[132] Jay Leftkowitz, a senior White House adviser who helped draft President Bush's stem cell policy, commented that the FDA policy will not be a barrier at this early stage of human ES cell research.[133] He says that years of basic research must be conducted before transplantation and the FDA regulations are even a relevant consideration and that, by that time, scientists will have found a way to comply with FDA guidelines.[134] It is worth noting however, that Mr. Leftkowitz's comments seem to imply that, at some time in the future, federal ES cell research funding policy would need to be changed to provide funding for research on cell lines propagated with FDA-compliant techniques.

In sum, while FDA xenotransplantation guidelines are of debatable importance at this early stage of human ES cell science, should researchers accomplish their goal of transforming human ES cells into transplantable products, these guidelines will be of paramount concern. While a broader approach to federal funding of human ES cell research would allow scientists to develop ES cell lines that are compliant with FDA guidelines, President Bush's stem cell policy does not allow this option. Scientists working under President Bush's plan would instead be forced to try to find ways to comply with FDA guidelines while using ES cell lines that had been exposed to mouse feeder cells and bovine serum, an endeavor that seems tenuous at best.

CONCLUSION

United States policy for federally funding human ES cell research needs to be broadened. By limiting federal funding to research on just seventy-eight ES cell lines, President Bush's plan will prevent ES cell researchers from reaching their end goal of using ES cell technology to create revolutionary medical treatments. If the taxpayers are going to fund ES cell research, they deserve the research to be funded in a way that will allow it to produce the benefits that they desire.

132. Gillis & Connolly, *supra* note 125.
133. *Id.*
134. *Id.*